REMARKS

Claims 21-37 have been withdrawn. Elected claims 1-20 are pending.

Claims 4, 7, 8, and 10 have been canceled.

Claim 1 has been amended to recite acceptable salts of N-acetyl-L-glutamine for use in the claimed composition, excluding aluminum salts. Support can be found in canceled claim 4.

Claims 2-20 have been amended to correct claim dependency.

Invention Synopsis

The liquid nutritional embodiments of the claimed invention are based upon the discovery that N-acetyl-L-glutamine has utility as an oral glutamine supplement in humans. It has now been found that human intestinal tissue deacetylates N-acetyl-L-glutamine, to thus form glutamine for use in the body. As such, N-acetyl-L-glutamine can now be incorporated into oral nutritionals designed for human consumption to thus provide a source of supplemental glutamine. This is especially useful in liquid formulations where N-acetyl-L-glutamine is more stable than free glutamine. Free glutamine is more commonly used in solid or powder product forms.

Applicants also found that orally administered N-acetyl-L-glutamine is a highly effective glutamine source, more so in many respects than even free glutamine itself.

Applicants conducted several studies to compare orally administered N-acetyl-L-glutamine, caseinate (protein source of glutamine), and glutamine (free glutamine). Initially, it was found that N-acetyl-L-glutamine absorption (pig small intestine) was comparable to that of free glutamine (see Figure 3). It was also found that portal blood levels of glutamine were similar between N-acetyl-L-glutamine and free glutamine after introduction of each into an isolated intestinal loop of pigs (Figure 3).

The data also show that orally administered N-acetyl-L-glutamine was more effective than glutamine on minimizing intestinal damage caused by protein-energy malnutrition in pigs. The deleterious effects of malnutrition on the antioxidant defense system in these pigs appeared less marked in the intestine of animals that orally consumed N-acetyl-L-glutamine (page 42, Example 4, lines 7-9). The data also show that oral N-acetyl-L-glutamine was

significantly more effective than free glutamine (oral) in reducing small intestine immunological changes promoted by malnutrition, especially in total cell number and B and T helper subpopulations (page 43, Example 4, lines 22-25).

FIGURE 7 shows electron transmission micrographs of jejunum enterocytes from healthy pigs (A, B panels) fed with ENSURE PLUS formula and protein-energy malnourished pigs fed with the same formula supplemented with caseinate (C, D panels), glutamine (E, F panels) or NAQ (G, H panels) for 30 days were analyzed for signs of inflammation, such as clear cytoplasmic spaces and lymphocyte infiltration.

FIGURE 8 shows electron transmission micrographs of ileum enterocytes from healthy pigs (A, B panels) fed with ENSURE PLUS formula and protein-energy malnourished pigs fed with the same formula supplemented with caseinate (C, D panels), glutamine (E, F panels) or NAQ (G, H panels) for 30 days were analyzed for signs of inflammation, such as clear cytoplasmic spaces and lymphocyte infiltration.

FIGURE 9 shows the effect of different compounds/products on the occurrence of apoptosis and inflammation on the mucosal of untreated celiac disease patients.

Restriction

In response to the restriction requirement set forth in the August 17, 2006 Office Action, Applicants' undersigned attorney hereby affirms the earlier telephonic election, without traverse, to pursue claims 1-20 (Group I) in the present application.

Rejections under 35 USC 112

Claims 2-20 have been rejected under 35 USC 112, second paragraph, as being indefinite for essentially reciting improper claim dependencies. Responsive to this rejection, the claims have been amended to recite proper claim dependencies.

Claims 7, 8, and 10 have also been rejected under 35 USC 112, second paragraph, as being indefinite for reciting non-limiting elements. Responsive to this rejection, claims 7, 8, and 10 have now been cancelled.

Accordingly, Applicant now request withdrawal of this rejection.

Obviousness Type Double Patenting Rejection

Claims 1-20 have been rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21 of commonly assigned US Patent 6,906,038 (Mazer), in view of any of JP 55-105652 (JP'652), JP 58-018320 (JP'320), or US 3,178,342 (Buzas), and further in view of US 6,572,898 (Nelson), US 5,489,440 (Ndife), and US 5,733,579 (Wolf). Applicant traverses this rejection.

Mazer claims a method to alleviate mucositis by administering an oral electrolyte solution comprising, per liter, 30-95 mEq of sodium, 10-30 mEq of potassium, and 10-40 mEq of citrate, and less than 3% by weight of a carbohydrate. Mazer fails to disclose N-acetyl-L-glutamine.

JP'652 discloses aluminum salts of N-acetyl-L-glutamine solutions to treat gastric ulcers. It fails to disclose any salt forms other than aluminum. It also fails to disclose oral electrolyte solutions.

JP '320 discloses N2-acetyl-L-glutamine-aluminum complex as an antiulcer agent. It fails to disclose any salt forms other than aluminum. It also fails to disclose oral electrolyte solutions.

US 3,178,342 (Buzas) discloses compositions containing acetylglutamic acid salt of dimethylaminoethanol (see Buzas, col. 1, lines 46-55), not N-acetyl-L-glutamine or any salt form thereof. This reference is therefore not relevant to patentability of the present claims.

US 6,572,898 (Nelson) discloses oral electroylte gels comprising, per liter, 20-60 mEq of sodium, 15-25 mEq of chloride, 20-50 mEq of citrate, and 20-30 g of carbohydrate, and 2-10 g of a structuring agent (column 3, lines 15-31). Nelson fails to disclose N-acetyl-L-glutamine.

US 5,489,440 (Ndife) discloses rice flour-based oral rehydration solutions (see abstract), e.g., solutions comprising water, rice flour, CMC, potassium choride, sodium citrate, citric acid, sodium chloride, neutrase, cellulase, flavors, and colors (see column 5, lines 15-30). Ndife fails to disclose N-acetyl-L-glutamine.

US 5,733,579 (Wolf) discloses oral rehydration solutions containing indigestible carbohydrates (see abstract). Wolf fails to disclose N-acetyl-L-glutamine.

Applicant respectfully submits that the Examiner has failed to establish a prima facia case of obviousness over claims 1-21 of US Patent 6,906,038 (Mazer) in view of any one or more of the secondary references. None of the references disclose a combination of an oral electrolyte solution with N-acetyl-L-glutamine. Applicants acknowledge that oral electrolyte solutions are known, as are compositions comprising N-acetyl-L-glutamine. However, Applicants can find no specific disclosure or teaching from any of the seven cited references to suggest such a combination.

Among the cited references, only JP'652 and JP'320 disclose compositions comprising N-acetyl-L-glutamine, and even then only as an aluminum salt. None of the of the other references disclose N-acetyl-L-glutamine in any context.

Among the cited references, only Mazer, Ndife, and Wolf disclose oral electrolyte solutions, none of which disclose or make any suggestion to add N-acetyl-L-glutamine.

Accordingly, Applicants request withdrawal of this rejection.

Rejection under 35 USC 103

Brouns in view of Nelson

Claims 1-3 and 5-18 have been rejected under 35 USC 103(a) as being unpatenable over EP 540 462 (Brouns) in view of US 6,572,898 (Nelson). Applicant traverses this rejection as it would apply to the amended claims.

Brouns discloses the use of L-glutamine, or derivatives, to prevent reduction of L-glutamine blood levels during exercise or other physical activity. Brouns references many different derivatives, including N-acetyl-L-glutamine (see p. 2, lines 22-46), but only exemplifies a composition comprising L-alanyl-L-glutamine, carbohydrate, fat, sodium, potassium, chloride, magnesium, calcium, and vitamins (see p. 4, lines 5-25). Brouns fails to disclose a formulation that actually contains N-acetyl-L-glutamine.

Nelson is summarized above.

Even if it were obvious to combine these prior art references, which Applicants maintain it is not, one of ordinary skill in the art would still not have expected that the N-acetyl-L-glutamine liquid composition when orally administered would be a highly effective glutamine source, more so in many respects than even free glutamine itself.

As noted above, Applicant conducted several studies to compare orally administered N-acetyl-L-glutamine, caseinate (protein source of glutamine), and glutamine (free glutamine). Initially, it was found that N-acetyl-L-glutamine absorption (pig small intestine) was comparable to that of free glutamine (see Figure 3). It was also found that portal blood levels of glutamine were similar between N-acetyl-L-glutamine and free glutamine after introduction of each into an isolated intestinal loop of pigs (Figure 3).

However, the data also show that orally administered N-acetyl-L-glutamine was more effective than glutamine on minimizing intestinal damage caused by protein-energy malnutrition in pigs. The deleterious effects of malnutrition on the antioxidant defense system in these pigs appeared less marked in the intestine of animals that orally consumed N-acetyl-L-glutamine (page 42, Example 4, lines 7-9). The data also show that oral N-acetyl-L-glutamine was significantly more effective than free glutamine (oral) in reducing small intestine immunological changes promoted by malnutrition, especially in total cell number and B and T helper subpopulations (page 43, Example 4, lines 22-25).

Applicant therefore submits that the presently claimed composition is patentably unobvious over the applied prior art in view of unexpected results as summarized above. Accordingly, Applicant requests withdrawal of this rejection.

Brouns in view of Nelson and JP'652, JP'320, or Buzas

Claims 4 has been rejected under 35 USC 103(a) as being unpatenable over EP 540 462 (Brouns) in view of US 6,572,898 (Nelson) and further in view of any one of JP 55-105652 (JP'652), JP 58-018320 (JP'320), or US 3,178,342 (Buzas).

Applicant traverses this rejection for the following reasons, including those given above in the traversal of the obviousness rejection over the combination of Brouns and Nelson. Applicants maintain that the claimed compositions, including claim 4, are supported by unexpected results as discussed above.

Moreover, as noted above, Buzas discloses compositions containing acetylglutamic acid salt of dimethylaminoethanol (see Buzas, col. 1, lines 46-55), not N-acetyl-L-glutamine or any salt form thereof. This particular reference is therefore not relevant to the patentability of the present claims.

As to the addition of the JP'320 and JP'320 references, they only disclose the use of N-acetyl-L-glutamine as an aluminum salt. The presently claimed compositions, as amended, recite a Markush listing of acceptable N-acetyl-L-glutamine salts, excluding aluminum salts.

Accordingly, Applicant requests withdrawal of this rejection.

Brouns in view of Nelson and Ndife

Claim 19 has been rejected under 35 USC 103(a) as being unpatenable over EP 540 462 (Brouns) in view of US 6,572,898 (Nelson) and US 5,489,440 (Ndife). Applicant traverses this rejection for the reasons given above in the traversal of the obviousness rejection over the combination of Brouns and Nelson. Applicants maintain that the claimed compositions, including claim 19, are supported by unexpected results as discussed above.

Accordingly, Applicant requests withdrawal of this rejection.

Brouns in view of Nelson and Wolf

Claim 20 has been rejected under 35 USC 103(a) as being unpatenable over EP 540 462 (Brouns) in view of US 6,572,898 (Nelson) and US 5,733,579 (Wolf). Applicant traverses this rejection for the reasons given above in the traversal of the obviousness rejection over the combination of Brouns and Nelson. Applicant maintains that the claimed compositions, including claim 20, are supported by unexpected results as discussed above.

Accordingly, Applicant requests withdrawal of this rejection.

Mazer in view of JP'652, JP'320, or Buzas

Claims 1-20 have been rejected under 35 USC 103(a) as being obvious over US 6,906,038 (Mazer) in view of any one of JP 55-105652 (JP'652), JP 58-018320 (JP'320), or US 3,178,342 (Buzas).

Applicant traverses this rejection for the reasons given above in the traversal of the obviousness-type double patenting rejection over claims 1-21 of US 6,906,038 (Mazer) in view of JP 55-105652 (JP'652), JP 58-018320 (JP'320), or US 3,178,342 (Buzas).

Applicant also traverses this rejection for the reasons given above in the traversal of the rejection of claims 1-3 and 5-18 under 35 USC 103(a) as being obvious over EP 540 462 (Brouns) in view of US 6,572,898 (Nelson). Applicant maintains that the claims 1-20 are supported by unexpected results as discussed above.

Accordingly, Applicant requests withdrawal of this rejection.

Conclusion

Applicants respectfully request reconsideration of this application and allowance of pending claims 1-20.

Respectfully submitted,

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